Sclerosing Foam in the Treatment of Varicose Veins and Telangiectases: History and Analysis of Safety and Complications

ALESSANDRO FRULLINI, MD, FACP AND ATTILIO CAVEZZI, MD

Studio Flebologico, Incisa Valdarno, Florence, and Clinica Stella Maris, S. Benedetto del Trunto (AP), Italy

OBJECTIVE. To review the use of sclerosing foam in the treatment of varicose veins, to describe the different techniques of foam preparation, and to report the complications of our 3-year experience with this treatment.

METHOD. From November 1997 to the end of October 2000, 453 patients were treated with a sclerosing foam for large, medium, and minor varicosities with sodium tetradecylsulfate (STS) or polidocanol (POL). A first group of 257 patients (90 for minor varicosities and 167 for medium to large veins) received a sclerosing foam according to the Monfreux technique. From December 1999 to October 2000, 196 patients were treated with a sclerosing foam prepared according to Tessari's method (36 for minor size veins or teleangectasias and 170 for medium-large veins). Every patient was studied with (color-flow) duplex scanning before and after the treatment and large vein injections were administered under duplex guide.

RESULTS. The immediate success rate was 88.1% in the first group for the medium-large veins. In the same districts we registered an early success rate in 93.3% for the patients treated with the Tessari's method. The complication rate (mostly minor complications) was 8.5% in the first group and 7.1% in the second group.

CONCLUSION. The use of sclerosing foam may become an established therapy in the treatment of varicose veins with a high success rate, low cost, and low major complication rate. According to our actual experience and knowledge, the safe amount of foam should not exceed the 3-ml limit, but further advancements could come from standardization of the foam preparation technique.

THE USE of sclerosing foam has been introduced in sclerotherapy with the aim of increasing the efficacy and safety of the treatment. In recent years many different techniques of foam production have been proposed.

The definition of a sclerosing foam (SF) is a mixture of gas and liquid sclerosing solution (detergent type) with tensio-active properties. The gas must be well tolerated or physiologic and the bubble size less than 100 μ. The behavior of sclerosing foam is different when injected, compared to the action of a liquid solution (Figure 1).

The use of air and a sclerosing drug in combination was described in 1944 by Orbach: the air block technique.[1] The sclerosing solution was added to air, simply shaking the syringe or the vial, with production of large bubbles which had a high air: liquid ratio and with increased efficacy only for smaller veins. The method was not suitable for larger veins where after the injection the air positioned itself along the upper side of the vein, impeding contact with endothelium.

Further advancement came then from subsequent innovations: Cabrera et al.[2] published an article about the production of a complex foam with CO_2 and an unknown tensio-active agent; In 1997, Monfreux[3] described the MUS method that generated a simple foam with air by means of a glass syringe; Mingo-Garcia[4] recently developed a special device to produce foam with compressed air; in 1998 Benigni and Sadoun published a method to produce a very short-lasting foam in a plastic syringe,[5,6] and in 1999 Tessari[7] presented an original method of foam production with two disposable syringes and a three-way tap.

In 2000 Frullini[8] published a different method that generated foam in a vial of sclerosing solution, provided that the vial has a rubber cap. The method was derived from the ideas of Lorenzo Tessari, and it utilizes the vortex effect that a disposable syringe and a relatively large connector can create into the vial with a fast push and pull action on the piston. With respect to the Monfreux method, Tessari's and Frullini's method may produce a foam with higher consistency, whereas the durability of the MUS foam is longer. Unfortunately long durability does not always mean good therapeutic effect because the latter is more correlated to high consistency for a minimum period of time in order to obtain optimal sclerosis. In the following article, the techniques will be discussed in more detail.

A. Frullini, MD, FACP and A. Cavezzi, MD, have indicated no significant interest with commercial supporters.

Address correspondence and reprint requests to: Alessandro Frullini, MD FACP, Via Einstein 2a, 50064 Incisa Valdarno, Florence, Italy. E-mail: alef@dada.it.

 • Published by Blackwell Publishing, Inc.
ISSN: 1076-0512/02/$15.00/0 • Dermatol Surg 2002;28:11–15

With these techniques excellent results have been reported in sclerotherapy of varicose veins by several authors (Cabrera,[2-9] Monfreux,[3] Henriet,[10,11] Sadoun and Benigni,[5,6] Mingo-Garcia,[4] Sica,[12] Cavezzi,[13] Tessari,[7] Frullini[14-16]) with excellent immediate occlusion rate and very few complications.

This article discusses the different methods of foam formation, our 3 year-experience with SF, and the possible future perspectives of this therapy. Moreover, we present our overall complication rate for 453 patients treated with foam.

Methods for Sclerosing Foam Production

The Monfreux Method

This method was initially reported by Monfreux in 1995, but he claims he has used it for many years. The foam is produced in a glass syringe filled with 0.3–0.5 ml of liquid. The tip of the syringe is then closed with a sterile plug and the operator must hold tension on the piston until 2–3 ml of foam are generated. A little training is required before using the technique to prepare a good quality foam. This SF is quite long lasting (even 3 h in vitro, probably up to 20 min in vivo) but it has a low consistency due to the relatively large diameter of the bubbles. Moreover, we demonstrated that the same technique and quantity of liquid can produce very different SF because it is very difficult to standardize this technique.

This technique has a higher rate of side effects. This is probably because of the large size of the bubbles which easily spread along the vessels. Patients sometimes experience dizziness or a confused state. These are self-limited side effects and they are of short duration. Even if the true nature of this symptom is still debatable (liquid drugs may generate similar symptoms), the best treatment is prophylaxis, asking the patient to lay on the office bed for about 5 min after the injection and avoiding excessive tension during foam generation in order to produce smaller bubbles. Another limitation with the Monfreux technique is the use of glass syringes, which may be a problem for doctors and patients and which require additional work for sterilization.

The Cabrera Method

In 1997 Juan Cabrera reported about his experience with a special foam prepared with POL or STS and an unknown tensio-active agent. The gas used was not air but CO_2 (or a different physiologic gas). Cabrera recently published the details and results of his technique (up to 7 years follow-up with excellent results). The technology for developing this SF is currently under development in the UK and it will probably be available in the future.

The Benigni-Sadoun Method

This method is based on the use of plastic syringes and repeated and fast pulling and release of the piston. The method generates a medium-quality foam, but very short-lasting.

The Garcia Mingo Method

Javier Garcia Mingo has developed a special device that uses compressed air to produce a foam suitable for sclerotherapy. We have no experience with this method and the only published experience is the one from the author.

The Tessari Method

In 1999 Lorenzo Tessari described an original method that uses two disposable syringes and a three-way tap to produce a high-quality foam with purified sodium tetradecylsulfate (STS). By this method the SF was produced by means of disposable material; later a dedicated kit was produced, in order to provide a prefilled syringe with sterile air. This made it possible to avoid the problems of using "nonsterile air" for injections and to avoid using glass syringes. This foam is very compact and with a very small bubble diameter. Another advantage is the ability to reconstitute the foam if the treatment session takes time to be completed.

The Frullini Method

In 2000 Frullini proposed a new technique for SF production. The mechanism of foam generation utilizes the same turbulence effect of the Tessari method. A

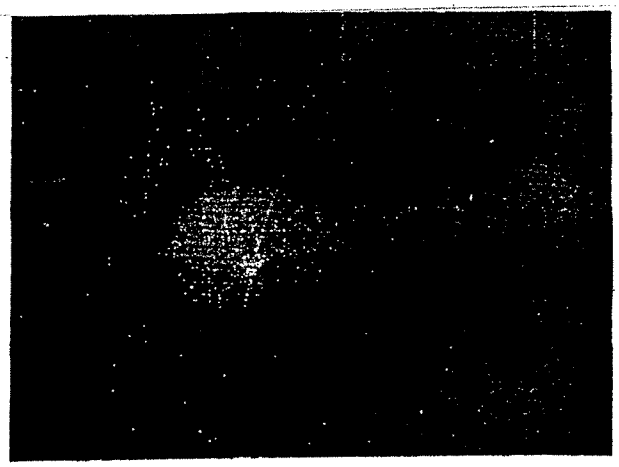

Figure 1. Sclerosing foam.

small connector is inserted in a 5 ml vial of STS with a rubber cap, preferably partially emptied. A 2.5 or 5 ml disposable syringe filled with a predetermined amount of air is then connected to the system and, after positioning the vial upside-down, quick injections/aspirations of solution are performed.

The foam can be aspirated for injections and reformed when needed, and, using a new syringe, the foam has the same consistency at reconstitution. The quality of the foam is related to the amount of air and liquid, the volume and type of syringe and (scarcely) the number of passages, providing a minimum of five passages.

Materials and Methods

We have retrospectively reviewed our experience using SF analyzing the medical records of the treated patients. From 1997 to 1999 we used the MUS technique, as described by Monfreux, in 167 medium or large veins. In the same period 90 treatments of telangiectases or reticular veins were administered with the same technique. On average, 1.8 sessions were necessary for medium or large vein obliteration, where STS was employed in 65% of cases and polidocanol (POL) in 35%, and five sessions on average were performed in the treatment of reticular varices or telangiectases where POL foam was employed. With the MUS technique we have never utilized more than 4 ml of foam, produced on average from 0.4 to 0.6 ml of liquid drug with a tension on the piston of the glass syringe for at least 1 minute.

From the end of 1999 until October 2000 we employed the Tessari technique in 196 patients using purified STS (87%); 26 patients were treated for minor varicosities and 170 for medium-large varicóse veins. The foam was generated with a three-way tap as described in the original technique. A mean of 2.7 ml of foam per session was employed. This was produced from 0.5 to 1.0 ml of STS 0.2–3% and 2–5 ml of air with 20 passages in the tap. The number of sessions ranged from one to six according to the aim of the treatment, with an average of 1.8 sessions being necessary for large veins.

During this 3-year experience with SF every patient was studied before the treatment with color-flow duplex investigation (CFDI) in the standing position, examining deep and superficial systems and perforators as well. Refluxes at the sapheno-femoral and sapheno-popliteal junction, or along the affected veins, were studied using the compression-release maneuver of the calf and the Valsalva test.

The treatments were administered by the authors and an eccentric compression using a pad and a class 1 (20–30 mmHg) or 2 (30–40 mmHg) elastic stocking was used during the daily period. When performing duplex-guided sclerotherapy for the long saphenous vein (LSV) or for inguinal recurrence (neovascularization), the compression was generally exerted only below the knee, except for those cases with grossly dilated varices at the thigh, whereas the compression involved the whole limb with pads (eccentric positive compression) over the varicose veins. In the treatment of telangiectases a 18-mmHg compression was generally employed.

Every patient was asked to walk nearly immediately after the injection and in the days after the treatment. One author (AC) left patients lying for about 5 min after the treatment session in order to increase foam contact with the veins and to possibly decrease its migration.

Complications were classified as systemic and local or as major (life-threatening) or minor.

In the posttreatment period every patient was investigated by physical examination and by CFDI, and in cases of clinically detectable complications (ie, varicophlebitis), the patient was followed up in the same manner until the recovery

Results

The overall result of foam sclerotherapy has been very good with an immediate success rate of 88.1% in the MUS technique group and 93.3% with the Tessari method (clinical and instrumental follow-up at 20–180 days).

In Tables 1 and 2, the complications of the two techniques are reported. The complication rate was lower in the patients treated with the Tessari method but a comparison between the two groups is not possible because of the mismatch in patient populations and the different areas treated. Moreover, the first part of our experience with the three-way tap method was used to create a standard technique and the complication rate at that time was higher due to the learning curve.

Table 1. Complications in 257 Patients Treated with Sclerosing Foam – MUS Method

Complication	*Cases*
Pigmentation	6
Varicophlebitis	5
Transient confusional status	3[a]
Transient visual disturbances	3
Partial popliteal dvt	1
Skin necrosis	4

[a]Twice in the same patient in different sessions.

Table 2. Complications in 196 Patients Treated with Sclerosing Foam, Tessari's Method

Complication	*Case*
Varicophlebitis	7
Malaise	1
Transient visual disturbance	1
Partial DVT(1 gastrocnemius vein thrombosis due to technical mistake and 1 popliteal thrombosis)	2
Lymphedema worsening	1
Skin necrosis	2

Discussion

The use of air in sclerotherapy was introduced by Orbach in 1944 with the air block technique. In his initial group of 297 patients he registered no gas embolism. Experimental experiences on animals in 1934 by Harkins and Harmon[17] and in 1937 by Richardson et al.[18] demonstrated the safety of a small amount of air injected in a relatively small period of time. In 1997 Henriet[15] revised these experiences and analyzed the passage of air in the general circulation in different conditions as extracorporeal circulation or during the gas-echocardiography used to study septal defects. In this technique an embolus of 5–10 ml of air is injected to demonstrate interatrial or interventricular defects. In his experience in 3200 sessions with a sclerosing foam (Monfreux's method) for minor varicosities, Henriet reported only a few minor complications and six side effects, possibly related to the use of air (three transient visual disturbances, two headaches, and one vomiting).

Our findings confirm that the use of an air sclerosing foam is as safe as liquid solution in terms of major complications (eg, pulmonary embolism, deep vein thrombosis, ischemic lesions, allergy, etc.), but it is our opinion that the total amount of foam injected per session should never exceed 3 ml, apart from very selective indications (ie, large saphenous stems, obese patients) and a minimum interval of 7 days between sessions should be respected. Future enhancements of the methods will allow the use of a larger amount of foam, and recent experiences of a few Australian colleagues (unpublished data) seem to favor large quantities of SF.

The advantages of sclerotherapy using SF are based on several theoretical and practical considerations. When the injection of a liquid sclerosant is performed, the concentration in the syringe is related to the dilution that will be obtained in the vein; it must be a high concentration because mixing with blood is unavoidable, leading to the action of a diluted drug on the endothelium. If the threshold level is reached, the sclerosing effect will start. This process is related to the concentration in the syringe, the volume of blood in which the drug will be diluted (which can be hardly judged from the diameter of the vessel), and the speed of injection.

We can think of an experimental model where 1 ml of 3% STS is injected with a needle in a 10-cm segment of vein containing 10 ml of blood. The final concentration of the active drug on the inner vessel wall will be 0.3%.

Using a foam prepared with STS 1%, injection in the same vein segment will push away the blood when the foam bolus reconstitutes in the vein. In this situation the foam will come in contact with the endothelium and the sclerosing effect is achieved.

When SF is injected the physics of the injection are completely different. The foam is made of tiny bubbles of gas "covered" by the tensio-active liquid. The latter is pure and the quantity of sclerosing drug in 1 ml of foam is related to the size of bubbles: with little bubbles, the foam will be highly active; large bubbles form poorly active foam. We should look at the sclerosis with foam as an active dynamic process; the interaction with endothelium forms links with cellular membranes and the higher the dose of drug per ml of foam, the higher the number of links between the SF and endothelium. Large bubbles of foam, even if it seems to last more in vitro, has a weaker effect because there is less sclerosing drug available for this linkage.

If we use SF, endothelial cells of large and minor veins should probably respond to the sclerosing agent at a given concentration in the same manner. The same concentration of sclerosing agent can be suitable for large and small veins (even saphenous stems of 6–10 mm have been successfully treated with low-concentration SF of purified STS) and this finding could change the decision-making process of sclerotherapy, due to the fact that lower concentrations and low doses of liquid could be used.

We can identify several peculiar properties of foam: adhesiveness, compactness, long lasting, echovisibility, enhancement of sclerosing power and reduction of drug doses and concentration. In fact, the SF adheres to the venous inner wall and with proper maneuvers it is possible to push the foam downward in collaterals and upward, close (not too close) to deep veins with low risk of propagation. The compactness is related to the size of the bubbles, and when this size is sufficiently small, no (or poor) mixing with blood occurs in the vein in the first moments after the injection; this results in a closer relationship between the injected dose and the final result.

The durability of the foam is related to bubble size, the tensio-activity of the liquid solution, and the conditions in which the SF is formed and kept. The air contained in the SF explains the echovisibility of the foam: in our opinion this is one of the biggest advantages when performing duplex-guided sclerotherapy, because it gives an enhanced view of the process, better identification of the injected flow, and the chance to push the SF in a safer way near the sapheno-popliteal or sapheno-femoral junction, or within the collaterals under direct visualization.

The increase in vein spasm generated by each injection is commonly reported by foam users and it may sometimes be dramatic with vein diameters that suddenly change from 15 mm to 3 mm. Another property of SF is the reduction of drug doses: 0.4–0.5 ml of liquid solution can be transformed in 2–2.5 ml of foam. Higher amounts of foam can be produced from the

same quantity of liquid according to the volume of air used, but the best dilution with the Tessari method, in our experience, is 1 to 4 or 1 to 5.

Conclusions

The use of sclerosing foam in the treatment of varicose veins is becoming an established therapy with a high immediate success rate, low cost, and low complication rate. Only a few non-randomized studies have been published and they have a short- or medium-term follow-up with good outcomes. Future studies are needed to elucidate the advantages of SF over liquid drug use in sclerotherapy, but our first outcomes highlight a major benefit from the use of SF, without any compromise of safety. Long-term results may show a recanalization rate similar or lower than traditional sclerotherapy outcomes, but the positive meaning of SF subsides in its low costs (low doses and low concentrations of drug), safety (extravasation of SF is less harmful than pure liquid), feasibility, and immediate sclerosis enhancement

The safe amount of injected air is, at the moment, 3 ml per session. Further experiences with more compact foam, smaller bubble size, or with other physiologic gases could probably increase the total amount of SF that could be safely injected. There is no large published experience at the moment with gases other than air in foam production and this prevents making judgments about other gases in sclerotherapy. The overall impression concerning sclerosing foam is in favor of enhanced sclerosing power, which should contribute to the diffusion of this technique, even expanding sclerotherapy indications for the treatment of varicose veins of the lower limbs. Other authors have used SF in the treatment of male varicocoele, pelvic congestion syndrome, and venous malformations.

The three cases of thrombus propagation in the deep vein system (even if one was due to a technical error) during duplex-guided sclerotherapy of short saphenous vein insufficiency suggest that the total amount of foam to be injected in this area should not exceed 1.5 or 2 ml; furthermore, additional precautions should be taken (ie, the slight elevation of the foot, with the patient in procumbent position, in order to lessen the chance of foam propagation in the deep venous system, and the execution of the uppermost injection far away from the sapheno-popliteal junction), as well as the high rate of minor complications (necrosis, pigmentation, vein inflammation) with SF in sclerotherapy of reticular varices and telangiectases seems to indicate a rearrangement concerning the use of SF in these cases; particularly in telangiectases injection, SF has demonstrated high efficacy, but local minor side effects can be explained with the augmented power of SF (if compared to liquid solution) and with the need for more information on the ideal procedure to manage sclerosing foam in the treatment of telangiectases.

References

1. Orbach EJ. Sclerotherapy of varicose veins: utilization of intravenous air block. Am J Surg 1944:362–6.
2. Cabrera Garrido JR, Cabrera Garcia-Olmedo JR, Garcia-Olmedo Dominguez MA. Elargissement des limites de la schlérothérapie: noveaux produits. Sclérosants Phlébologie 1997;50:181–8.
3. Monfreux A. Traitement sclérosant des troncs saphènies et leurs collatérales de gros calibre par la méthode. MUS Phlébologie 1997; 50:351–3.
4. Mingo-Garcia J. Esclerosis venosa con espuma: Foam Medical System. Revista Española de Medicina y Cirugía Cosmética 1999;7: 29–31.
5. Benigni JP, Sadoun S, Thirion V, Sica M, Demagny A, Chahim M. Télangiectasies et varices réticulaires. Traitement par la mousse d'Aetoxisclérol a 0,25%. Présentation d'une étude pilote. Phlébologie 1999;52:283–90.
6. Sadoun S, Benigni JP. The treatment of varicosities and teleangectasias with TDS or Lauromacrogol foam. Abstract of XIII World Congress of Phlebology, Sydney 6–11 September. 1998:327.
7. Tessari L. Nouvelle technique d'obtention de la sclero-mousse. Phlébologie 2000;53:129.
8. Frullini A. New technique in producing sclerosing foam in a disposable syringe. Dermatol Surg 2000;26:705–6.
9. Cabrera Cabrera J Jr, Garcia-Olmedo MA. Treatment of varicose long saphenous veins with sclerosant in microfoam form: long term outcomes. Phlebology 2000;15:19–23.
10. Henriet JP. un an de pratique quotidienne de la sclérothérapie (veines reticulaires et téleangiectasies) par mousse de polidocanol. Faisabilité, Résultats, Complications. Phlébologie 1997;50:355–60.
11. Henriet JP. Expérience durant trois années de la mousse de polidocanol dans le traitement des varices réticulaires et des varicosités. Phlébologie 1999;52:277–82.
12. Sica M, Benigni JP. Echosclerose à la mousse: trois ans d'expèrience sur les axes saphéniens. Phlébologie 2000;53:339–42.
13. Cavezzi A, Frullini A. The role of sclerosing foam in ultrasound guided sclerotherapy of the saphenous veins and of recurrent varicose veins. Aust NZ J Phlebol 1999;3:49–50.
14. Frullini A, Cavezzi A. Ultrasound guided sclerotherapy treatment of long saphenous vein insufficiency. In (eds E. Rabe, et al. Phlebology, 99-Ed Viavital Verlag GmbH-Cologne.)., 1999: p 142–3.
15. Frullini A, Cavezzi A. Echosclérose par mousse de tétradécyl-sulfate de sodium et de polidocanol: deux années d'expérience Phlébologie 2000;53–4:431–5.
16. Frullini A, Cavezzi A, Tessari L. Scleroterapia delle varici degli arti inferiori mediante schiuma sclerosante di Fibro-vein® con il metodo Tessari: esperienza preliminare. Acta Phlebologica 2000;1:43–8.
17. Harkins HN, Harmon PN. Embolism by air and oxygen: comparative studies. Proc Soc Exp Biol Med 1934;32:178.
18. Richardson HF, Coles BC, Hall GE. Experimental gas embolism: intravenous air embolism. Toronto Can Med Assoc J 1937;36:584–8.